AMENDMENTS TO THE CLAIMS:

1. (**Currently Amended**) A method of tag-directed synthesis of a plurality of compounds **wherein a nucleic acid tag directs and encodes the synthesis of a compound to which it is covalently attached**, comprising:

(a) ~~forming a first group of subsets of nucleic acid tags for participating in a first synthetic reaction step from a pool of nucleic acid tags~~ **providing a pool of subsets of nucleic acid tags**, wherein each nucleic acid tag comprises **a single stranded DNA sequence having a 5' terminus and** a first **variable** hybridization sequence linked to a second **variable** hybridization sequence, **wherein said 5' terminus is covalently attached to a chemical reaction site,** ~~which said second hybridization sequence is linked to a chemical reaction site~~, **and wherein each of said first and second variable hybridization sequences is different for each subset of nucleic acid tags;**

(b) splitting the pool of nucleic acid tags of step (a) to form a first group of subsets of nucleic acid tags for participating in a first synthetic reaction, by contacting said nucleic acid tags with a plurality of first immobilized nucleotide sequences, each designed to capture a subset of said nucleic acid tags by **specific** hybridization between one of said first **variable** hybridization sequences and ~~the~~ **and one of said** first immobilized sequence**s, and physically separating the subsets of said pool of nucleic acid tags on the basis of said first variable hybridization sequence of each nucleic acid tag and removing said first immobilized sequence**;

~~(b)~~ **(c)** carrying out the first synthetic **reaction** ~~step~~ by reacting the chemical reaction sites of the nucleic acid tags in each of the subsets formed in ~~(a)~~ **step (b)** with a selected one of a plurality of first reagents **that couples a different chemical subunit** to ~~convert~~ the chemical reaction site of each subset of nucleic acid tag**s under conditions effective** to **form** a reagent-specific compound intermediate to produce **a first group of** subsets of reacted nucleic acid tags;

~~(c)~~ **(d)** pooling the **first group of** subsets of reacted nucleic acid tags **of step (c) to form a first pool of reacted nucleic acid tags**;

~~(d)~~ **(e) splitting the first pool of reacted nucleic acid tags of step (d) to** ~~forming~~ **form** a second group of subsets of ~~the pooled~~ reacted nucleic acid tags ~~of step (c),~~ for

participation in a second synthetic reaction step, by contacting said ~~pooled~~ **first pool of** reacted nucleic acid tags with a plurality of second immobilized nucleotide sequences, each designed to capture a subset of said **first pool of** reacted nucleic acid tags by **specific** hybridization between one of said second **variable** hybridization sequences and the second immobilized sequence**, and physically separating the subsets of said first pool of reacted nucleic acid tags on the basis of said second variable hybridization sequence of each nucleic acid tag and removing said second immobilized sequence**; and

~~(e)~~ **(f)** carrying out the second synthetic **reaction** ~~step~~ by reacting the reagent-specific compound intermediate of the reacted nucleic acid tag in each of the subsets formed in ~~(d)~~ **step (e)** with a selected one of a plurality of second reagents **that couples a different chemical subunit to the reagent-specific compound intermediate of each subset of reacted nucleic acid tags formed in step (e) under conditions effective to form a different sequence oligomer or different sequence small-molecule compound attached to a nucleic acid tag to produce a second group of subsets of reacted nucleic acid tags, whereby a plurality of compounds is produced**.

2. (**Cancelled**)

3. (**Currently amended**) The method of claim 1, ~~for use in forming a plurality of oligomers with different subunit sequences,~~ wherein the plurality of first and second reagents in steps ~~(b)~~ **(c)** and ~~(e)~~ **(f)** include different oligomer subunits.

4. (**Currently amended**) The method of claim 1, ~~for use in forming a plurality of compounds with different substituents,~~ wherein the plurality of first and second reagents in steps ~~(b)~~ **(c)** and ~~(e)~~ **(f)** include different **small molecule** compound substituents.

5. (**Currently amended**) The method of claim 1 for making a plurality of compounds requiring more than 2 synthetic steps wherein the **second group of subsets of reacted** nucleic acid tags **produced in step (f) is subjected to one or more additional rounds of (*i*) pooling to form an Nth pool of reacted nucleic acid tags, (*ii*) splitting to form an Nth group of subsets of reacted nucleic acid tags, and (*iii*) synthesis to produce subsets of Nth**

reacted nucleic acid tags, and wherein each round includes an additional step-specific subset of **Nth variable** hybridization sequences **and Nth immobilized nucleotide sequences** for each synthetic step N greater than 2 and which further comprises, for each additional synthetic step N;

~~(f)~~ **(g) forming an Nth pool of reacted nucleic acid tags, wherein each of said nucleic acid tags of step (a) comprises said Nth variable hybridization sequence linked to said second variable hybridization sequence, and wherein each of said first, second and Nth variable hybridization sequences is different for each subset of nucleic acid tags;**

(h) splitting the Nth pool of reacted nucleic acid tags of step (g) to ~~forming~~ **form** an Nth group of subsets of reacted nucleic acid tags for participating in ~~the~~ **an** Nth reaction step, by contacting said **Nth pool of reacted** nucleic acid tags with a plurality of **said** Nth immobilized nucleotide sequences, each designed to capture a subset of said **reacted nucleic acid** tags by **specific** hybridization between one of said ~~tag~~ Nth **variable** hybridization sequences and the Nth immobilized sequence**, and physically separating the subsets of said Nth pool on the basis of said Nth variable hybridization sequence of each reacted nucleic acid tag and removing said Nth immobilized sequence**;

~~(g)~~ **(i) carrying out the Nth reaction step by** reacting the ~~compound intermediates~~ **the reacted nucleic acid** ~~in the~~ tags in each of the subsets formed in ~~(f)~~ **step (h)** with a **selected** one of a plurality of Nth-reaction reagents **that couples a different chemical subunit to the different sequence oligomer or different sequence small-molecule compound of each subset formed in step (h) under conditions effective to produce subsets of Nth reacted nucleic acid tags**; and

~~(h)~~ **(j)** repeating steps ~~(f) and (g)~~ **(g) - (i)** if necessary, until synthesis of the compounds is complete.

6. (**Currently amended**) The method of claim 5 wherein each subset of nucleic acid tags includes at least 5 separate **variable** hybridization sequences.

7. (**Currently amended**) The method of claim 1, wherein said nucleic acid tags within each subset further comprises for each subset of **variable** hybridization sequences, an adjacent **constant** spacer sequence separating that **variable** hybridization sequence from an adjacent one, each of said **constant** spacer sequences being the same for all subsets of nucleic

acid tags and each **variable** hybridization sequence being different for each group of subsets of nucleic acid tags.

8. (**Previously presented**) The method according to claim 1, for use in enriching the plurality of compounds for those having a desired compound activity, further comprising identifying from said plurality of compounds, one or more compounds having a desired activity to yield a subpopulation of nucleic acid tags, and using the subpopulation to carry out the method of claim 1.

9. (**Currently amended**) The method according to claim 8, wherein said using **the subpopulation** includes;

amplifying said subpopulation of nucleic acid tags by polymerase chain reaction (PCR), **and**

adding a chemical reaction site~~, and~~

~~using said amplified subpopulation having chemical reaction sites to carry out the method of claim 1~~.

10. (**Currently amended**) The method ~~according to~~ **of** claim 7, ~~for use in producing new permutations of active compounds wherein said nucleic acid tags have one of a plurality of spacer sequences,~~ **wherein** each of said **constant** spacer sequences ~~having~~ **comprises** a unique restriction enzyme site**, and wherein the method further comprises:**

~~(f)~~ **(g)** identifying from said plurality of compounds, one or more compounds having a desired activity to yield a subpopulation of nucleic acid tags;

(h) amplifying said subpopulation of nucleic acid tags by polymerase chain reaction (PCR);

~~(g)~~ **(i)** treating said subpopulation of nucleic acid tags with one or more restriction enzymes under conditions effective to produce a partial digest;

~~(h)~~ **(j)** rejoining said partially digested nucleic acid tags; **and**

~~(i)~~ **(k)** adding a new chemical reaction site to said partially digested nucleic acid tags and using the subpopulation to carry out the method of claim 1.

11.-14. (**Canceled**)

15. (**Previously presented**) The method of claim 1, wherein each of said first and second immobilized nucleotide sequences are each bound to the surface of a solid phase reagent.

16. (**Currently amended**) The method of claim 1, wherein said steps ~~(b)~~ **(c)** and ~~(c)~~ **(f)** include first transferring the ~~separate~~ subsets of said nucleic acid tags from said immobilized sequences to a solid support prior to said reacting.

Please add the following new claims:

17. (**Newly presented**) The method of claim 1, wherein said chemical reaction site is covalently attached to said 5' terminus through a linker.

18. (**Newly presented**) The method of claim 1, wherein said chemical reaction site is a chemical component capable of forming a chemical bond selected from amide, ester, urea, urethane, carbon-carbonyl bonds, carbon-nitrogen bonds, carbon-carbon single bonds, olefin bonds, thioether bonds, and disulfide.

19. (**Newly presented**) The method of claim 1, wherein said chemical subunits are amino acids.

20. (**Newly presented**) The method of claim 19, wherein said chemical reaction site is a primary amine, said amino acids are Fmoc-protected amino acids, said reacting couples a selected Fmoc-protected amino acid to said primary amine to form an amide bond, and said reacting is followed by removal of the Fmoc protecting group of said selected Fmoc-amino acid prior to a next reacting step.

21. (**Newly presented**) The method of claim 20, wherein said reagent-specific compound intermediate is an amino acid presenting a new primary amine ready for a next reacting step.

22. (**Newly presented**) The method of claim 7, wherein said variable hybridization sequences and said constant spacer sequences are catenated nucleotide sequences each at least 10 nucleotides long, and wherein said nucleic acid tag includes at least 5 variable hybridization sequences.

23. (**Newly presented**) A method for the iterative synthesis and screening of a plurality of compounds to produce a subpopulation of compounds having a desired activity, wherein a nucleic acid tag directs and encodes the synthesis of the compound to which it is covalently attached, said method comprising:

(a) providing a pool of subsets of the nucleic acid tags in which each nucleic acid tag comprises a single stranded DNA sequence having a 5' terminus and a first variable hybridization sequence linked to a second variable hybridization sequence, wherein said 5' terminus is covalently attached to a chemical reaction site, and wherein each of said first and second variable hybridization sequences is different for each subset of nucleic acid tags;

(b) splitting the pool of nucleic acid tags of step (a) to form a first group of subsets of nucleic acid tags for participating in a first synthetic reaction, by contacting said nucleic acid tags with a plurality of first immobilized nucleotide sequences, each designed to capture a subset of said nucleic acid tags by specific hybridization between one of said first variable hybridization sequences and one of said first immobilized sequences, and physically separating the subsets of said pool of nucleic acid tags on the basis of said first variable hybridization sequence of each nucleic acid tag and removing said first immobilized hybridization sequence;

(c) carrying out the first synthetic reaction by reacting the chemical reaction sites of the nucleic acid tags in each of the subsets formed in step (b) with a selected one of a plurality of first reagents that couples a different chemical subunit to the chemical reaction site of each subset of nucleic acid tags under conditions effective to form a reagent-specific compound intermediate to produce a first group of subsets of reacted nucleic acid tags;

(d) pooling the first group of subsets of reacted nucleic acid tags of step (c) to form a first pool of reacted nucleic acid tags;

(e) splitting the pool of the first group of reacted nucleic acid tags of step (d) to form a second group of subsets of reacted nucleic acid tags for participation in a second synthetic

reaction step, by contacting said first pool of reacted nucleic acid tags with a plurality of second immobilized nucleotide sequences, each designed to capture a subset of said first pool of reacted nucleic acid tags by specific hybridization between one of said second variable hybridization sequences and the second immobilized sequence, and physically separating the subsets of said first pool on the basis of said second variable hybridization sequence of each nucleic acid tag and removing said second immobilized sequence;

(f) carrying out the second synthetic reaction by reacting the reagent-specific compound intermediate of the reacted nucleic acid tag in each of the subsets formed in step (e) with a selected one of a plurality of second reagents that couples a different chemical subunit to the reagent-specific compound intermediate of each subset of reacted nucleic acid tags formed in step (e) under conditions effective to form a different sequence oligomer or different sequence small-molecule compound to produce a second group of subsets of reacted nucleic acid tags;

(g) subjecting the second group of subsets of reacted nucleic acid tags produced in step (f) to one or more additional rounds of (*i*) pooling to form an Nth pool of reacted nucleic acid tags, (*ii*) splitting to form and Nth group of subsets of reacted nucleic acid tags, and (*iii*) synthesis to produce subsets of Nth reacted nucleic acid tags, wherein each round includes an additional step-specific subset of Nth variable hybridization sequences and Nth immobilized nucleotide sequences, and wherein each additional round comprises:

(h) forming an Nth pool of reacted nucleic acid tags, wherein each of said nucleic acid tags of step (a) comprises said Nth variable hybridization sequence linked to said second variable hybridization sequence, wherein each of said first, second and Nth variable hybridization sequences is different for each subset of nucleic acid tags;

(i) splitting the Nth pool of reacted nucleic acid tags of step (h) to form an Nth group of subsets of reacted nucleic acid tags for participating in an Nth reaction step, by contacting said Nth pool of reacted nucleic acid tags with a plurality of said Nth immobilized nucleotide sequences, each designed to capture a subset of said reacted nucleic acid tags by specific hybridization between one of said Nth variable hybridization sequences and the Nth immobilized sequence, and physically separating the subsets of said Nth pool on the basis of said Nth variable hybridization sequence of each reacted nucleic acid tag and removing said Nth immobilized sequence;

(j) carrying out the Nth reaction step by reacting the reacted nucleic acid tags in each of the subsets formed in step (h) with a selected one of a plurality of Nth-reaction reagents that couples a different chemical subunit to the different sequence oligomer or different sequence small-molecule compound of each subset formed in step (h) under conditions effective to produce subsets of Nth reacted nucleic acid tags;

(k) repeating steps (h) - (j) if necessary, until synthesis of a plurality of compounds is complete;

(l) identifying from said plurality of compounds of step (k), one or more compounds having a desired activity to yield a subpopulation of nucleic acid tags; and

(m) producing a pool of nucleic acid tags based on the subpopulation of nucleic acid tags from step (l) and repeating steps (a) – (l) if necessary, until synthesis of a plurality of compounds having the desired activity is complete.

24. (**Newly presented**) The method of claim 23, wherein said chemical reaction site is covalently attached to said 5' terminus through a linker.

25. (**Newly presented**) The method of claim 23, wherein said chemical reaction site is a chemical component capable of forming a chemical bond selected from amide, ester, urea, urethane, carbon-carbonyl bonds, carbon-nitrogen bonds, carbon-carbon single bonds, olefin bonds, thioether bonds, and disulfide.

26. (**Newly presented**) The method of claim 23, wherein said chemical subunits are amino acids.

27. (**Newly presented**) The method of claim 26, wherein said chemical reaction site is a primary amine, said amino acids are Fmoc-protected amino acids, said reacting couples a selected Fmoc-protected amino acid to said primary amine to form an amide bond, and said reacting is followed by removal of the Fmoc protecting group of said selected Fmoc-amino acid prior to a next reacting step.

28. (**Newly presented**) The method of claim 27, wherein said reagent-specific compound intermediate is an amino acid presenting a new primary amine ready for a next reacting step.

29. (**Newly presented**) The method of claim 23, wherein said nucleic acid tags within each subset further comprises for each subset of variable hybridization sequences, an adjacent constant spacer sequence separating that variable hybridization sequence from an adjacent one, each of said constant spacer sequences being the same for all subsets of nucleic acid tags and each variable hybridization sequence being different for each group of subsets of nucleic acid tags,

30. (**Newly presented**) The method of claim 29, wherein said variable hybridization sequences and said constant spacer sequences are catenated nucleotide sequences each at least 10 nucleotides long, and wherein said nucleic acid tag includes at least 5 variable hybridization sequences.